

U.S. Application No. 09/874,141
Attorney Ref. No. 037003-0280632

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Canceled)

2. (Currently amended) An improved method of treating an autoimmune disease or disorder treatable by inhibiting gp39 expression or the interaction of human gp39 with CD40, wherein said method comprises

obtaining anti-human gp39 antibodies;

assaying to identify anti-human gp39 antibodies that inhibit the ~~gp39-CD40~~ interaction of human gp39 with CD40;

assaying to identify anti-human gp39 antibodies that compete for binding to human gp39 with murine antibody 24-31, produced by hybridoma cells assigned ATCC accession no. HB-11712;

assaying to identify anti-human gp39 antibodies that are ~~substantially~~ non-agonistic of a human T-cell activation response selected from the group consisting of T-cell proliferation, the production of interleukin 2 (IL-2), the production of interleukin-4 (IL-4) and the production of interferon γ (IFN- γ);

identifying anti-human gp39 antibodies that inhibit the ~~gp39-CD40~~ interaction of human gp39 with CD40, compete with murine antibody 24-31 for binding to human gp39, and are ~~substantially~~ non-agonistic of said human T-cell activation response; and

administering a therapeutically effective amount of said anti-human gp39 antibodies that inhibit the ~~gp39-CD40~~ interaction of human gp39 with CD40, compete with murine antibody 24-31 for binding to human gp39, and are substantially non-agonistic of said human T-cell activation response.

3. (Currently amended) The improved method of claim 2 wherein said disease or disorder is characterized by induction of IL-2 production, and the anti-human gp39 antibodies that are administered are ~~substantially~~ non-agonistic of IL-2 production by human T cells.

4. (Canceled)

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5. (Previously presented) The improved method of claim 2, wherein said autoimmune disease or disorder is selected from the group consisting of rheumatoid arthritis, psoriasis, multiple sclerosis, diabetes, systemic lupus erythematosus and idiopathic thrombocytopenic purpura.

6-15. (Canceled)

16. (Previously presented) The improved method of claim 2, wherein said autoimmune disease or disorder is multiple sclerosis.

17. (Previously presented) The improved method of claim 2, wherein the anti-gp39 antibodies that are administered are chimeric or humanized antibodies having constant regions of human antibodies.

18. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered are chimeric "primatized"[®] antibodies having light and heavy chain variable regions of an antibody of an Old World monkey, and constant regions of human antibodies.

19. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered are humanized antibodies.

20. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered have heavy chain constant regions from a human antibody of isotype selected from gamma-1, gamma-3, and gamma-4.

21. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered comprise a light or heavy chain that has at least one conservative amino acid substitution.

22. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered comprise a heavy chain constant region having an amino acid substitution selected from the group consisting of
replacement of leucine with glutamic acid at Kabat position 236, and
replacement of serine with proline at Kabat position 229.

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23. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies that are administered bind to the same epitope of gp39 as murine antibody 24-31, produced by hybridoma cells assigned ATCC accession no. HB-11712.

24. (Previously presented) The improved method of claim 23, wherein the anti-gp39 antibodies comprise the complementarity determining regions of the 24-31 antibody light and heavy chain variable regions shown in Figure 7 (SEQ ID NO:27) and Figure 8 (SEQ ID NO:28), respectively.

25. (Previously presented) The improved method of claim 24, wherein the anti-gp39 antibodies comprise:

a humanized light chain variable region comprising an amino acid sequence selected from the group consisting of:

DIVMTQSPSFLSASVGDRVITTC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT
GVPDRFSGSGSGTDFTLTISLQPEDFADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:1)

DIVMTQSPDSLAVSLGERATINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT
GVPDRFSGSGSGTDFTLTISLQAEDVADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:2)

DIVMTQSPSFMSTSVGDRVITTC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT
GVPDRFSGSGSGTDFTLTISMQPEDFADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:3) and

DIVMTQSPDSMATSLGERVTINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT
GVPDRFSGSGSGTDFTLTISMQAEDVADYFC QQYNSYPYT FGGGTKLEIK; (SEQ ID NO:4)

and a humanized heavy chain variable region comprising an amino acid sequence selected from the group consisting of:

EVQLQESGPGLVKPSQTLSTCTVSGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS
RISISRDTSKNQFSLKLSSVTAADTGVIYCAC RSYGRTPYYFDF WGQGTTTLTVSS; (SEQ ID NO:5)

EVQLQESGPGLVKPSQTLSTCTVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS
RISISRDTSKNQFSLKLSSVTAADTGVIYCAC RSYGRTPYYFDF WGQGTTTLTVSS; (SEQ ID NO:6)

EVQLQESGPGLVKPSQTLSTCAVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS
RISISRDTNNQFSLNLNSVTRADTGVIYCAC RSYGRTPYYFDF WGQGTTTLTVSS; (SEQ ID NO:7) and

EVQLQESGPGLVKPSQTLSTCAVYSGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS
RISISRDTSKNQFYLKLSSVTAADTGVIYCAC RSYGRTPYYFDF WGQGTTTLTVSS. (SEQ ID NO:8)

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26. (Previously presented) The improved method of claim 25, wherein the anti-gp39 antibodies that are administered have heavy chain constant regions from a human antibody of isotype selected from gamma-1, gamma-3, and gamma-4.

27. (Previously presented) The improved method of claim 25, wherein the anti-gp39 antibodies that are administered comprise a light or heavy chain that has at least one conservative amino acid substitution.

28. (Previously presented) The improved method of claim 25, wherein the anti-gp39 antibodies that are administered comprise a heavy chain constant region having an amino acid substitution selected from the group consisting of
replacement of leucine with glutamic acid at Kabat position 236, and
replacement of serine with proline at Kabat position 229.

29. (Canceled)

30. (Currently amended) The improved method of claim 2, wherein the step of screening to identify anti-human gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of a T-cell activation response comprises assaying to determine the effect of an anti-human gp39 antibody on the production of a cytokine by human T cells selected from IFN- γ , IL-4, and IL-2.

31. (Canceled)

32. (Currently amended) The improved method of claim 30, wherein the anti-human gp39 antibodies that are administered inhibit the gp39-CD40 interaction and are ~~substantially~~ non-agonistic of production by human T cells of a cytokine selected from IFN- γ , IL-4, and IL-2.

33. (Currently amended) The improved method of claim 2, wherein the step of screening to identify anti-human gp39 antibodies that inhibit the gp39-CD40 interaction and are substantially non-agonistic of a human T-cell activation response comprises assaying to determine the effect of an anti-human gp39 antibody on human T cell proliferation.

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34. (Currently amended) The improved method of claim 33, wherein the anti-human gp39 antibodies that are administered inhibit the gp39-CD40 interaction and do not stimulate human T cell proliferation

35. (Previously presented) The improved method of claim 2, wherein the anti-gp39 antibodies are administered parenterally.

36. (Previously presented) The improved method of claim 17, wherein the anti-gp39 antibodies are administered parenterally.

37. (Previously presented) The improved method of claim 17, wherein the dosages of anti-gp39 antibodies that are administered are in the range of 0.05 to 100 mg per kilogram body weight per day.

38. (Previously presented) The improved method of claim 37, wherein the dosages of anti-gp39 antibodies that are administered are in the range of 0.5 to 10 mg per kilogram body weight per day.